

The University of Chicago

ABSORPTION OF LIQUID
PETROLATUM ("MINERAL OIL")
FROM THE INTESTINE
A HISTOLOGIC AND CHEMICAL STUDY

A DISSERTATION SUBMITTED TO THE FACULTY
OF THE DIVISION OF THE BIOLOGICAL SCIENCES
IN CANDIDACY FOR THE DEGREE OF DOCTOR OF
PHILOSOPHY

DEPARTMENT OF PATHOLOGY

1940

By
WALTER A. STRYKER

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ABSORPTION OF LIQUID PETROLATUM ("MINERAL OIL") FROM THE INTESTINE

A HISTOLOGIC AND CHEMICAL STUDY

WALTER A. STRYKER, M.D., PH.D.

CHICAGO

The use of liquid petrolatum (medicinal "mineral oil") as a laxative for real or fancied intestinal stasis was popularized chiefly through the recommendations of Sir W. Arbuthnot Lane¹ in the first decade of the twentieth century. Liquid petrolatum is one of several products obtained from petroleum by distilling off the more volatile products, chilling, purification by filtration through bone, etc. According to the process of preparation, products of various consistencies are obtained, varying from waxy paraffin to the liquid mineral oil of household use. The latter consists of hydrocarbons of the methane and related aliphatic series; the medicinal product (liquid petrolatum) commonly used in this country consists chiefly of the saturated hydrocarbons. The earliest internal use of refined petrolatum probably dates to 1872, when Robert A. Chesebrough,² of New York, was granted a patent for the manufacture of "a new and useful product from petroleum, named vaseline." In the period prior to 1900 Randolph³ and others⁴ published occasional reports advocating the use of liquid petrolatum but it was not until this product was lauded in the widespread articles of Lane, supported by his position as chief surgeon of Guy's Hospital, that there was general acceptance. In 1914 the Council on Pharmacy and Chemistry of the American Medical Association⁵ discussed liquid petrolatum and suggested standards for the various types of the oil. During the years since then the popularity of this product has been increasingly widespread until at the present time it is unusual to find any person who has not occasionally used liquid petrolatum.

From the Department of Pathology, University of Chicago.

1. Lane, W. A.: *Brit. M. J.* **2**:1125, 1913.

2. Chesebrough, R. A., cited by Council on Pharmacy and Chemistry.⁵

3. Randolph, N. A.: (a) *Proc. Acad. Nat. Sc., Philadelphia* (1884), 1885, p. 281; (b) *Therap. Gaz.* **9**:732, 1885

4. (a) Hutchison, R.: *Brit. M. J.* **1**:724, 1899. (b) Robinson, W. D.: *M. News, New York* **77**:55, 1900.

5. Liquid Petrolatum or "Russian Mineral Oil," report of the Council on Pharmacy and Chemistry, *J. A. M. A.* **62**:1740, 1914.

From the first the question of the absorption of the oil was of interest. Experimental work designed to determine whether the material passed in toto through the intestinal canal or was partially taken into the body was done on human subjects and on animals. Such experiments were of two main types: The first consisted of feeding a certain amount of liquid petrolatum to the subject and then determining how much could be recovered from the feces or from the lymph stream containing ingested products. The second method, used chiefly by later workers, involved a search in the tissues of the animal body for ingested hydrocarbon after the latter had been fed to the animal. In general, the results from the first method were interpreted to indicate that liquid petrolatum was not absorbed, and the results from the second, that some absorption probably did occur.

REVIEW OF THE LITERATURE

The first recorded attempts to determine experimentally the absorption of liquid petrolatum were reported by Randolph,^{3a} in 1884. He fed 2 healthy adults 30 cc. of "vaseline" (probably petrolatum) over a period of forty-eight hours. The alvine discharges for the next three days were collected, dried and extracted with purified petroleum benzine (petroleum ether). "Making a slight allowance for incompleteness in extraction, the vaseline ingested was in each case recovered in its totality, showing that it has passed through the economy unchanged and unabsorbed." In 1889 Hutchison^{4a} published similar results. He fed a human subject 7 Gm. of liquid petrolatum and recovered 7.2 Gm. of unsaponifiable material. He concluded that the excess was probably due to traces of soaps. One year later Robinson^{4b} made the following assertion: "That every minim swallowed passed unchanged entirely through the intestinal tract of man was repeatedly proven. Nature evidently made no effort towards its digestion or assimilation." No details of the work by which these conclusions were reached were given. In the same year a report of the first experimental work in which animals were used was published by Henriques and Hausen.⁶ An emulsifiable mixture of petrolatum and lard was fed to rats, and 98 per cent of the liquid petrolatum was recovered from the feces. From this the conclusion was drawn that liquid petrolatum could not be absorbed. Continuing the use of human adults as experimental subjects, Schmidt⁷ fed up to 20 Gm. of liquid petrolatum at one time without observing any injurious effect. He was unable to recover from the feces the entire quantity of the product administered and believed that a certain portion of it, probably the fractions with low boiling points, were absorbed or possibly oxidized in the organism.

The most detailed experiments of this first type (analysis of the feces for material fed) were reported by Bloor⁸ as part of his studies on the absorption of fats. In his first group of experiments, solutions of unemulsified hydrocarbon oils were fed to cats and the amount of unabsorbed oils determined by extraction of the feces. The amount of recovered material ranged from 85.5 to 102.5 per cent of

6. Henriques, V., and Hausen, C.: *Centralbl. f. Physiol.* **14**:313, 1900.

7. Schmidt, A.: *München. med. Wchnschr.* **52**:1970, 1905.

8. Bloor, W. R.: *J. Biol. Chem.* **15**:105, 1913.

the amount fed. His conclusions were: "The recovery of the hydrocarbon jelly was practically complete as was also that of the hydrocarbon oil when fed alone, while there was a slight discrepancy in the recovery of the hydrocarbon oil when fed in solution in olive and coconut oils which may have been due to absorption. Taking into account, however, the error of the experiment, the amount absorbed was probably negligible. The possibility of absorption of these substances either in solution in fats or fatty acids or in the form of emulsions is shown to be extremely unlikely."

Another general method of experimental approach used in this problem consisted, as has been stated, in the study of the contents of the lymphatics draining the intestines after the hydrocarbon has been fed. Bradley and Gasser⁹ fed a dog an emulsified mixture of olive oil and liquid petrolatum and found in the thoracic lymph both oils in about the same relative proportion as in the emulsion which had been fed. This suggested to them a mechanical absorption of droplets of mixtures of fatty acid and hydrocarbon oil. Bloor⁸ repeated these experiments but with opposite results. The unsaponifiable material which he recovered from the chyle fat was believed to be chiefly cholesterol, and he concluded that "the amount and nature of the unsaponifiable matter precludes the possibility of the absorption of any appreciable amount of the hydrocarbon oil. The results . . . give no grounds for the belief that these substances are absorbed from the intestine."

Gage and Fish¹⁰ studied the digestion, absorption and assimilation of fat in man and animals by observing fat particles ("chylomicrons") in the circulating blood by means of the dark field microscope and a fat-soluble dye. Testing the digestibility of castor oil and liquid petrolatum (on man?), they found that "there was no increase in the chylomicrons, and we interpret the findings to mean that no digestion of either substance took place. There was no purgative action until after the actual period for the digestion of fatty food; therefore, both the substances were in the intestine a sufficient time for thorough digestion. When mixed with butter, the mineral oil is left behind but the butter fat is picked out, digested and absorbed." Mellanby¹¹ carried on experiments similar to those of Bloor but used bile as the emulsifying agent. The cat was used as the experimental animal. Examination of the intestine and mesentery during a period of six hours showed that there was no absorption of petroleum into the lymphatic system of the intestine, although the oil passed rapidly down the intestine. The method of examination was not reported.

Both of the general methods described are of value only for indicating absorption of a large proportion of ingested oil. For study of the possible absorption of small amounts, more delicate methods are necessary. The experiments of Channon and Collinson¹² were of this type. These workers studied the unsaponifiable fractions of the livers of animals which had received liquid petrolatum in their diet, comparing the iodine number of this fraction with that of the livers of animals receiving the control diet only. Rats and swine were used as the experimental animals, and similar results were attained with each. The rats were maintained on a diet containing 5 per cent liquid petrolatum for five weeks; the yield of unsaponifiable matter from the livers of the animals which had received the oil was increased by 40 per cent over that of the control groups, while the iodine

9. Bradley, H. C., and Gasser, H. S.: *J. Biol. Chem.* **11**:xx, 1912.

10. Gage, S. H., and Fish, P. A.: *Am. J. Anat.* **34**:1, 1924.

11. Mellanby, J.: *J. Physiol.* **64**:xxxiii, 1927.

12. Channon, H. J., and Collinson, G. A.: *Biochem. J.* **23**:676, 1929.

value of the nonsterol portion (cholesterol removed by digitonin) was 30.8 in the group fed oil and 118.8 in the control group. Two pigs were used: One was given the control diet and the other the same diet plus 100 cc. daily of liquid petrolatum emulsified with acacia. The animals were killed after fifty-four days. The comparative iodine values here were 36.6 for the animal fed the oil and 112.8 for the control animal. Other determinations (acetyl value, percentage of bromine in the brominated product) gave similar results. In a discussion of the possible mechanism by which the oil was absorbed, the authors suggested that in spite of much contrary evidence particulate absorption may occur.

Twort and Twort¹³ reported the first histologic changes thought to be due to hydrocarbons. After application of liquid petrolatum (the product was called "mineral oil" in the article but in a subsequent report was designated as "medical liquid paraffin") to the skin of mice, the livers were found to show first periportal infiltration by small round cells; the cells later became larger, with eccentric nuclei, called by them "endotheloid-xanthomatoid." These cells underwent disintegration with formation of foamy cytoplasm and later coarse vacuolation with ultimate replacement by a globule of fat. Whether this fat was of a saponifiable or a hydrocarbon nature could not be stated. Similar cells were occasionally seen in the spleen, adrenals and ovary. The authors believed that the oil had access to the internal organs by the alimentary tract, with the animals ingesting the oil from the skin. The condition developed also in rabbits and rats. No further reports have appeared to indicate their conclusions as to the nature of the condition. Tantini¹⁴ published the results of experiments in which he fed liquid petrolatum by mouth to guinea pigs for a four month period. He stated that the oil could be demonstrated in the hepatic cells, where it could be differentiated from the other fat by the Carminati method. The oil was said to produce lesions of a regressive nature in these cells, distributed focally, with a preference for the centers of lobules. No lesions were seen in the intestine or in other organs studied (pancreas, spleen). An example of histopathologic change in man was reported by Jaffé.¹⁵ Histologic examination of an appendix removed from a woman with the symptoms of acute appendicitis showed tissue similar to that seen in paraffinoma, including giant cells. The contents of the cells stained red with scarlet red, and chemical analysis was said to reveal liquid petrolatum. No further details were given.

It is the current practice to teach that liquid petrolatum is not absorbed from the intestine. Thus the textbook of pharmacology by Sollmann¹⁶ states "Mineral oils are not absorbed (except perhaps doubtful traces: Bradley and Gasser, 1912), but are eliminated unchanged in the feces (Randolph, 1885; Hutchison, 1899; Bloor, 1913)." Similar statements have been made by Cushny,¹⁷ Clark,¹⁸ Bastedo,¹⁹

13. Twort, C. C., and Twort, J. M.: *Lancet* **1**:448, 1932; *J. Hyg.* **33**:396, 1933.

14. Tantini, E.: *Tumori* **9**:266, 1935.

15. Jaffé, R. H.: *Deutsche med. Wchnschr.* **60**:508, 1934.

16. Sollmann, T.: *A Manual of Pharmacology*, ed. 5, Philadelphia, W. B. Saunders Company, 1936.

17. Cushny, A.: *A Textbook of Pharmacology and Therapeutics*, ed. 11, Philadelphia, Lea & Febiger, 1936.

18. Clark, A. J.: *Applied Pharmacology*, ed. 6, Philadelphia, P. Blakiston's Son & Co., 1938.

19. Bastedo, W. A.: *Materia Medica, Pharmacology and Therapeutics*, ed. 3, Philadelphia, W. B. Saunders Company, 1932.

McGuigan²⁰ and Beckman²¹ and in "Useful Drugs."²² In 1937 the Council on Foods of the American Medical Association,²³ in a discussion of the use of mineral oil in foods, stated, "It is well known that liquid petrolatum is not absorbed from the gastrointestinal tract," but the statement was qualified by a footnote calling attention to the work of Channon and Collinson. The results just reviewed seem to indicate that such qualifications are necessary. While the earlier types of experimentation did indicate that there was no marked absorption of the hydrocarbons, the methods were not of use in detecting minimal absorption. For this, experiments similar to those of Channon and Collinson plus histologic studies of the type described by Twort and Twort and by Tantini are necessary.

STATEMENT OF THE PROBLEM

In the routine autopsy studies of this laboratory lesions have been observed in various tissues which it was thought might be due to the ingestion of liquid petrolatum. The present investigation was devised to determine whether absorption of this oil occurs, and, if so, what type of lesions result.

MATERIAL AND METHODS

For the experimental part of the problem rabbits, rats and guinea pigs were used. Four brands of liquid petrolatum were employed: 1. Heavy white mineral oil (Sonneborn), from Pennsylvania fields. This oil is stated to be completely saturated; it has a specific gravity of 0.875 to 0.885. 2. Light white mineral oil (Sonneborn), similar in composition to the heavy type, but with a specific gravity of 0.860 to 0.870. 3. McKesson's albolene. 4. Russian mineral oil (Walgreen Drug Stores). No differences were noted to depend on the type of oil used. When the animals died or were killed after selected intervals of time, complete autopsies were done. In every case blocks of the intestine, mesenteric lymph nodes, liver and spleen were fixed in Zenker's solution, and sections made and stained with hematoxylin and eosin. In addition, in some instances, histologic examinations of other organs were made. In many of the discussions of pneumonia due to liquid petrolatum, the failure of reduction of osmic acid has been considered a specific reaction to indicate the type of oil present. While it is true that this method would differentiate liquid petrolatum from animal or vegetable neutral fats and fatty acids, it would not prove the absence of cholesterol, phosphatides or cerebro-sides, none of which reduce the acid. These are the lipids characteristic of the lipid storage diseases, and thus a means of differentiation from them is essential. Further, it has been shown²⁴ that the use of osmic acid on tissue fixed in solution of formaldehyde U. S. P. is likely to lead to false interpretations, since after such fixation certain lipoprotein combinations often reduce the acid. However, the stain is of corroborative value, and as such it has been used. For the specific

20. McGuigan, H. A.: Applied Pharmacology, St. Louis, C. V. Mosby Company, 1940.

21. Beckman, H.: Treatment in General Practice, ed. 3, Philadelphia, W. B. Saunders Company, 1938.

22. Useful Drugs, ed. 11, Chicago, American Medical Association, 1938.

23. Mineral Oil in Foods, report of the Council on Foods, J. A. M. A. **109**: 1814, 1937.

24. Hoerr, N. L.: Anat. Rec. **66**:149, 1936.

detection of liquid petrolatum in tissues, the method of Carminati²⁵ has been recommended. This stain is based on a difference in the solubility of orange sudan G in liquid petrolatum as compared with other lipids or oils. The results obtained with this method, however, are not completely satisfactory. If no sudanophilic material other than liquid petrolatum is present, a good contrast may be achieved between the oil, staining yellow, and the surrounding tissues. However, normal saponifiable fats, as in adipose tissue, or pathologic fats, as in fatty metamorphosis in the liver, may with the Carminati method stain either orange or yellow or in some cases may stain yellow centrally and orange peripherally. Further, while the stain may be of some value if the material stained is in large drops, when it is in small droplets or in cells there is insufficiently sharp differentiation. This difficulty is especially noted in sections of the liver where the hepatic cells and the red blood cells also stain yellow with orange sudan G. Thus the stain was found to be of most value in the differential staining of intestinal mucosa and mesenteric lymph nodes and was of less value in the examination of the liver and spleen unless the liquid petrolatum was in relatively sharply demarcated aggregations of macrophages. Where the differential staining by the Carminati method was most marked, the sudan IV (scarlet red) stain likewise showed differences between the staining of saponifiable fats and that of liquid petrolatum, the latter being light orange and the former dark orange. There is the possibility that this difference depends on the quantity of material present to be stained. All the specific fat stains were used on gelatin-embedded material.

The macrophages containing liquid petrolatum have a characteristic appearance, which was found to be nearly as valuable a means of identification as the stains used. There is marked variance in the size of adjacent droplets. Some are definitely intracellular but even here variable in size; there is not the homogeneous appearance of the alimentary lipophages, of the fatty macrophages of the lipoid storage diseases or of the brown fat of the lower animals, nor are there the single large drops of neutral fat found in the normal mature fat cell. Many of the drops of oil appear to be extracellular, and giant cells of the type often found as a reaction to a foreign body are frequently seen about them. In all the tissues the oleophages tend to occur in aggregations, but isolated cells are also seen. It will be noted that this appearance is characteristic of the reaction to liquid petrolatum in other tissues, such as the lungs in lipid pneumonia, the subcutaneous tissues in paraffinoma, the pleura following oleothorax due to the injection of liquid petrolatum and the peritoneum in the reaction following the intraperitoneal injection of liquid petrolatum.

In the microscopic examination of the tissues of the animals and of the autopsy material from human subjects a comparative grading scheme was adopted with values of + to +++++, depending on the quantities of oleophages and extracellular oil present.

Chemical analyses of the tissues were made in an attempt to recover any liquid petrolatum that might be present in the various organs. The microscopic examination would show the location of any ingested hydrocarbon, while the chemical analysis would offer supplementary but more definite proof of the presence of the substance. These analyses were of tissues from the experimental animals and from control animals of similar ages. The unsaponifiable fats and oils were determined, the saturated hydrocarbons isolated and a comparison made of the amounts of material thus obtained from experimental and control animals. A more detailed description of the process is given later.

25. Carminati, V.: *Sperimentale*, Arch. di biol. **88**:564, 1934.

In addition to this experimental work, autopsy material was studied to determine whether any absorption of liquid petrolatum occurred in the human subject. Sections of the intestines, mesenteric lymph nodes, liver and spleen were examined in such cases as they were available. Routine sections of the intestines, mesenteric lymph nodes, liver and spleen were also studied from 25 consecutive autopsies of bodies over 21 years of age at Albert Merritt Billings Hospital regardless of the history. Microscopic examinations and chemical analyses of these tissues were made when indicated and possible.

DETAILS OF EXPERIMENTS

Thirteen adult white rabbits, 21 albino rats and 31 guinea pigs were fed varying amounts of liquid petrolatum.

The rabbits were fed the regular stock laboratory diet consisting of Alpha flakes²⁶ with frequent supplements of carrots and lettuce. The chosen amount of liquid petrolatum to be given the animal was poured over the top of the flakes; the animals ate these oil-covered flakes as readily as the dry flakes. The dosage of oil was 20 cc. or 30 cc. daily; the duration of the feeding varied, with the longest period thirteen months.

Two groups of rats were used. The fifteen animals of the first group were fed white bread over which liquid petrolatum had been poured. Supplements of carrots and lettuce were given. This method of feeding did not permit measurement of the quantity of oil ingested by each rat. The duration of feeding of the rats varied up to nineteen months. The 12 rats of the second group were divided into two subgroups of 6 animals each. Each subgroup was fed the stock laboratory breeding diet, but 5 per cent of light liquid petrolatum was added to the food of one subgroup. The rats were fed their respective diets for six weeks and then were killed. The livers of these animals were chemically analyzed; this portion of the problem was a repetition of the work of Channon and Collinson.

The guinea pigs were fed the same diet as were the rabbits. The animals received the chosen amount of liquid petrolatum by means of a 1 cc. tuberculin syringe; the glass end of the syringe was placed in the animal's mouth and as large a quantity of oil as the animal would swallow at one time was delivered. The quantity of oil fed the guinea pigs varied from 1 cc. to 20 cc. daily; the duration of the feeding ranged up to fifteen months.

Most of the animals were killed and examined within a few days after the final feeding of the liquid petrolatum.

RESULTS OF EXPERIMENTS

Gross Findings.—At autopsy the rabbits fed the oil for periods of seven months or less did not show gross changes that could be ascribed to the liquid petrolatum. The animals fed a longer time had in their intestines numerous 1 mm.-sized white nodules, elevated about 1 mm. above the surrounding mucosa; these were most conspicuous in the jejunum and the first portion of the colon. The mesenteric lymph nodes were enlarged, and on their surfaces were similar small white nodules. An occasional nodule could be seen in the liver.

26. The formula for alpha flakes is given by the manufacturer as: protein not less than 15 per cent, fat not less than 3 per cent, fiber 12 per cent, carbohydrate 62 per cent, alfalfa, oats, barley, corn, soybean meal, whole wheat, dry buttermilk, linseed oil meal, salt, calcium carbonate and calcium sulfate.

Rats fed liquid petrolatum longer than seven months showed a similar involvement of their mesenteric lymph nodes. In their livers were numerous yellow flecks, which appeared to be distributed according to the location of the portal triads. Lesions were not seen in the intestines.

The guinea pigs did not have gross changes in any of their tissues.

Microscopic Observations.—Intestines: Changes considered to be the result of the feeding of liquid petrolatum were found in the intestines of the rabbits; such changes were not seen in the intestines of the rats or the guinea pigs. The lesions found in the rabbits were essentially of the same type in all the animals, but their extent increased with the length of time liquid petrolatum had been fed. If an animal had been fed this oil for a comparatively short time (e. g., four months), the vacuolated cells were seen in the lamina propria, most abundant in the jejunum but present also in the colon. The intracellular vacuoles varied in size, but most of them were comparatively large; occasionally the large ones were surrounded by smaller vacuoles. There was a tendency for several of the vacuoles to be in apposition. The larger number of these oleophages were in the superficial lamina propria near the tips of the villi in the jejunum, but occasional vacuoles were present in the deeper portions. If an animal had been fed the oil for a longer time (e. g., thirteen months), the sections of the jejunum, ileum and colon showed vacuolated cells in the same locations but much more numerous. In addition, interspersed among these cells were larger vacuoles that appeared to be extracellular and often were bordered by giant cells. In some sections of jejunum, the entire lamina propria at the tip of the villus was replaced by these two types. In the ileum, similar cells and vacuoles were seen in the intestinal lymphatic follicles.

Sections of intestine stained with sudan IV stain for fat showed sudanophilic material in those areas in which the vacuoles and vacuolated cells were seen in the sections stained with hematoxylin and eosin. The material stained a light orange in contrast to the orange-red color of the adjacent adipose tissue. With osmic acid, this material in the mucosa showed no reduction, while the adipose tissue was black. With the Carminati stain, the mucosal material was stained yellow, while the adipose tissue was orange.

Mesenteric Lymph Nodes: All three species of animals used had intracellular and extracellular vacuoles in their mesenteric lymph nodes. The extent of the lesions was again related to the length of time the liquid petrolatum had been fed. The earliest change seen in the nodes of the rabbits was the appearance in nearly every medullary cord of accumulations of large and small vacuoles, both intracellular and extracellular. These were similar to those seen in the intestine but were more numerous than in the intestine of the same animal and showed more variation in size. About some of the vacuoles an elongated

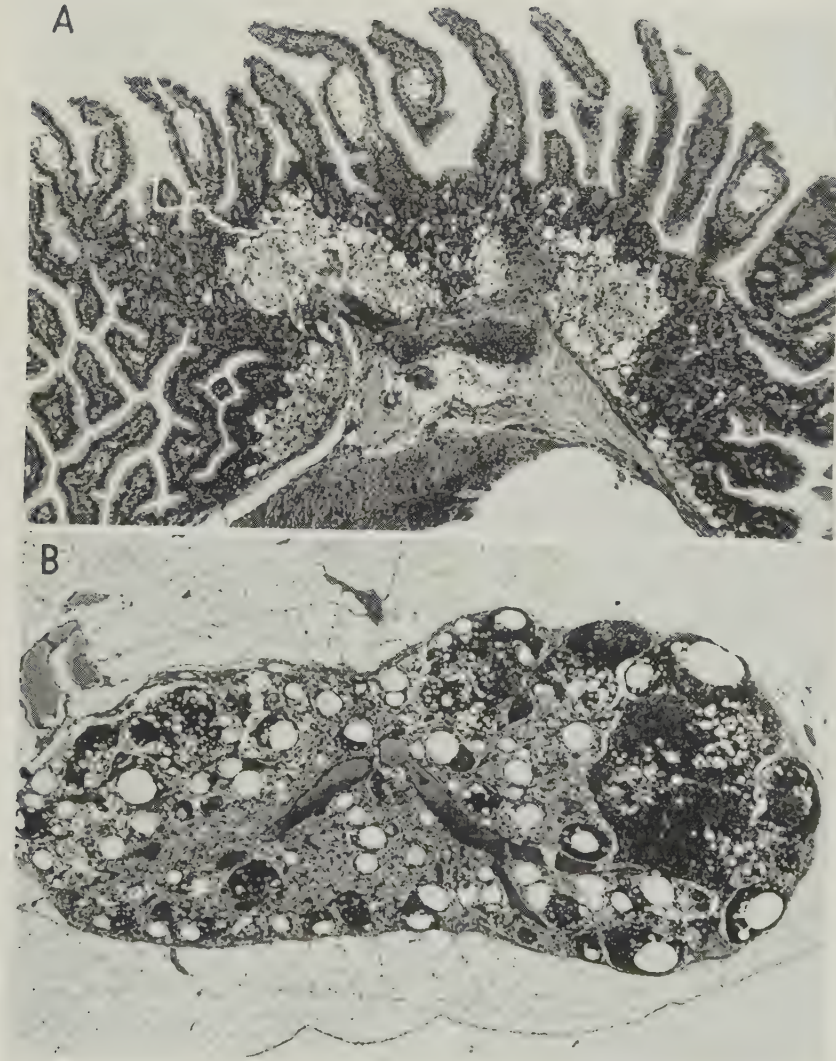


Fig. 1.—*A*, jejunum of rabbit fed liquid petrolatum for thirteen months. Numerous oleophages and extracellular collections of the oil are in the lamina propria. $\times 44$. *B*, mesenteric lymph node of the same rabbit. The oil is located in the follicles and medullary cords. $\times 20.5$.

crescentic nucleus could be seen. In these early stages only an occasional oleophagocyte or extracellular vacuole was seen in the large peripheral mass of lymphatic tissue. No giant cells were found about the larger central vacuoles. In animals fed a longer period, however, poorly formed giant cells were present. In these nodes nearly all the lymphatic follicles, as well as the medullary cords, contained large numbers of the vacuolated cells and the extracellular vacuoles. The infiltration of the follicles and cords had distended those structures and placed the walls of the sinuses in apposition so that the outlines of the sinuses were difficult to ascertain.

The mesenteric lymph nodes of the rats showed similar changes, again varying according to the length of time the animal had received the oil. Giant cells were not seen. In the mesenteric lymph nodes of those rats of the second group which had been fed liquid petrolatum for only six weeks, a few scattered vacuolated cells were seen in the medullary cords; in the peripheral follicles of some of the nodes there were scattered nests of mononuclear cells with nonvacuolated eosinophilic cytoplasm. In the nodes of animals fed for nineteen months the intracellular and extracellular vacuoles were so numerous that in many places they had displaced nearly all the lymphatic tissue, so that only a small ring of lymphocytes outlined the former site of the cord or follicle. In other parts large numbers of lymphocytes remained.

The tissues of guinea pigs fed liquid petrolatum for a period of less than seven months did not show lesions. The mesenteric lymph nodes of some of the animals fed a longer time had occasional vacuolated cells and extracellular vacuoles in the medullary cords and peripheral follicles. These lesions had the morphologic appearance of those described in the lymph nodes of the rabbits and the rats.

Frozen sections of the mesenteric lymph nodes of all three species of animals were stained for fat. The results of the use of osmic acid and orange sudan G were not unequivocal in all sections, but the largest part of the sudanophilic material in the vacuolated cells and extracellular vacuoles did not reduce osmic acid and was yellow with the Carminati stain.

Liver: Lesions appeared in the livers later than in the lymph nodes. As in the other tissues, the extent of the lesions was related to the length of time the oil had been fed to the animal. It is possible that some of the earliest lesions were not recognized, because of a lack of clear differentiation from other pathologic changes in the hepatic tissue. The first lesion noted was the appearance adjacent to a few of the triads of occasional isolated vacuolated cells, in which the vacuoles varied in size; these cells resembled the cells in the intestines and mesenteric lymph nodes. The cells were neither numerous nor conspicuous. In the liver of a rabbit fed for a long time numerous vacuolated cells were scattered

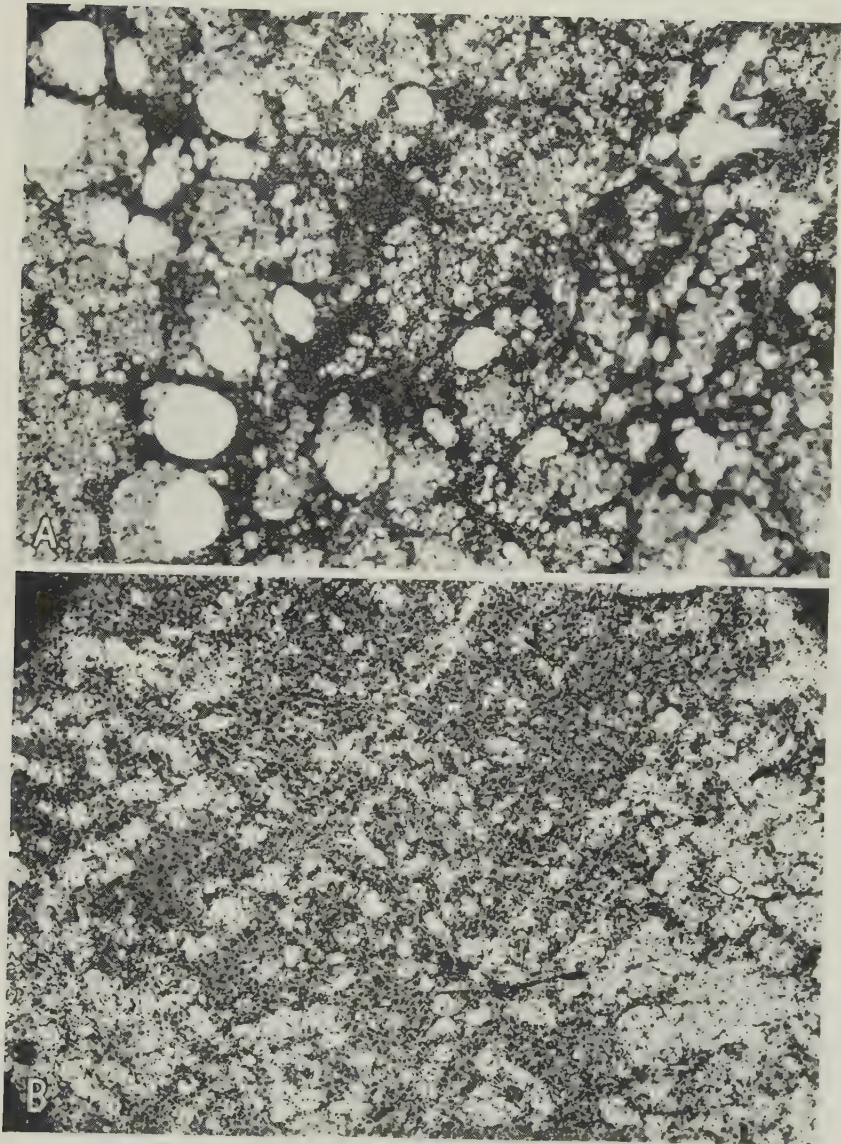


Fig. 2.—*A*, mesenteric lymph node of a rat fed liquid petrolatum for nineteen months. $\times 97$. *B*, liver of the same rat. The macrophages containing the oil are located throughout the lobules; the majority are periportal. $\times 75$.

irregularly throughout the lobules but most abundantly in the periportal areas. About some of these were small collections of lymphatic cells. These oleophages were again similar in structure to those seen in the intestines and in the mesenteric lymph nodes; they were not as well differentiated from the surrounding parenchymatous cells as were the similar cells in the other tissues.

In rats fed for a sufficient period the lesions were similar to those in the rabbit but more marked. Practically every triad was surrounded by large and small aggregations of vacuolated cells and extracellular vacuoles. These were both in the tissue of the triad and adjacent to the triads, where they had apparently replaced the liver parenchyma. Similar individual cells were scattered irregularly throughout the more central portions of the lobules. Giant cells were not seen.

In some of the sections of the livers of the guinea pigs a few vacuolated cells were seen adjacent to triads. In frozen sections the content of these cells appeared to be yellow with the Carminati stain, but there was insufficient contrast with the other tissues for evaluation. Since most of the livers of the guinea pigs showed marked fatty metamorphosis, no certain microscopic demonstration of liquid petrolatum was possible.

In many of the frozen sections of the livers of the rabbits and rats which were stained for fat no evaluation of the sudanophilic material present could be made by use of osmic acid or orange sudan G; the amount of material present was insufficient for differentiation. Where a large amount was present, however, globules corresponding to the vacuoles considered to indicate liquid petrolatum in the hematoxylin-eosin sections failed to reduce osmic acid and were yellow when stained by the Carminati method.

Other Tissues: Only one other tissue contained vacuolated cells. In the spleen of a rat fed for a long period many scattered small nests of oleophages were seen. All vacuoles here were intracellular. Many of these nests were definitely in the malpighian bodies; others were in the vicinity of arteries and trabeculae and may have been in the sites of former follicles from which the lymphocytes had been displaced. The material in the cells in the frozen sections did not reduce osmic acid and was yellow with the Carminati stain. Sections of the spleens of the rabbits and guinea pigs did not show such changes.

Other Lesions: Two other lesions of note were found. Leukemic infiltrations were present in all tissues examined from a rat that had been fed for a comparatively long period. Grossly, this leukemic tissue was green. In some of the guinea pigs fed over a long period there was infiltration of the submucosa and muscular coats of the intestines by vacuolated cells resembling adipose tissue; in frozen sections the con-

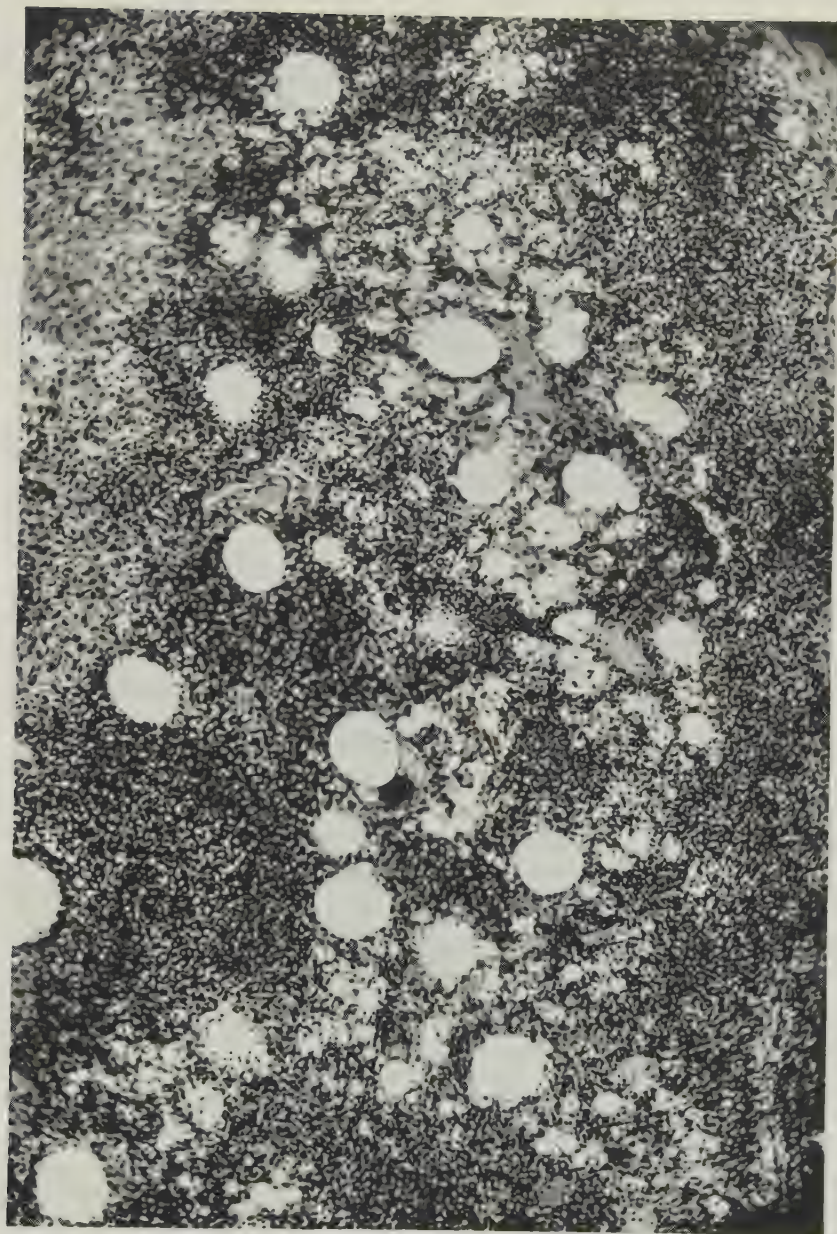


Fig. 3.—Mesenteric lymph nodes in case 2. There was a clinical history of the use of liquid petrolatum. Note the giant cell with vacuolated cytoplasm. $\times 110$.

tents of these cells reduced osmic acid and stained orange with the Carminati stain. All other pathologic changes were those frequently seen in the three species of animals used.

Comment.—Although the absorption of liquid petrolatum was demonstrable in all three groups of animals used, there were interesting differences. In the rabbits intestinal lesions were a conspicuous feature; such lesions were absent in the rats and guinea pigs. Giant cells were seen only in the rabbit; the oil was seen in the spleen only in the rat. In all animals the ease of the demonstration of the oil and the quantity present were related to the length of time the material had been fed.

The evaluation of changes was more difficult in the case of the guinea pig than in that of the rabbit or that of the rat. It would appear that the oil was not absorbed as rapidly. This may have been related to the different method of feeding; the oil was administered in one dose daily, separate from the food. It was impossible to train the guinea pigs to eat a diet in which the oil and the food had been mixed. When other changes in the liver were absent, material appearing to give the staining reactions for liquid petrolatum could be shown, but the fat stains were of no value in the presence of generalized fatty metamorphosis. In general, in all the animals staining methods were of value only when relatively large quantities of oil were present.

It was also noted in the work with guinea pigs that not only was a sufficient period required before changes could be noted but also a relatively large quantity of the oil was necessary. The absorption was related to both factors; certain animals fed comparatively small amounts showed no changes although they were fed longer than six months, while 1 animal was fed 1,500 cc. of oil in six months without microscopic evidence of change.

HUMAN AUTOPSY MATERIAL

The material which was studied in order to observe the incidence of typical oleophages in human tissues was either the routine autopsy material of the department of pathology of the University of Chicago or special material taken at routine autopsies performed by members of the department. Sections of mesenteric lymph nodes are usually not made unless the prosector feels that there is some definite indication for the microscopic examination, and thus such sections were available in less than 15 per cent of the cases. In a series of slightly over 400 autopsies, however, there were at least 23 instances in which oleophages considered to be typical of the absorption of liquid petrolatum were present in the mesenteric lymph nodes. In 7 of these cases similar vacuolated cells were found also in the liver and spleen. Since sections of the intestines are taken for microscopic examination only when such study seems indicated at the time of autopsy, intestinal material was available in only 12 of the 23 cases. Oleophages were found in 1 of these 12 cases. In

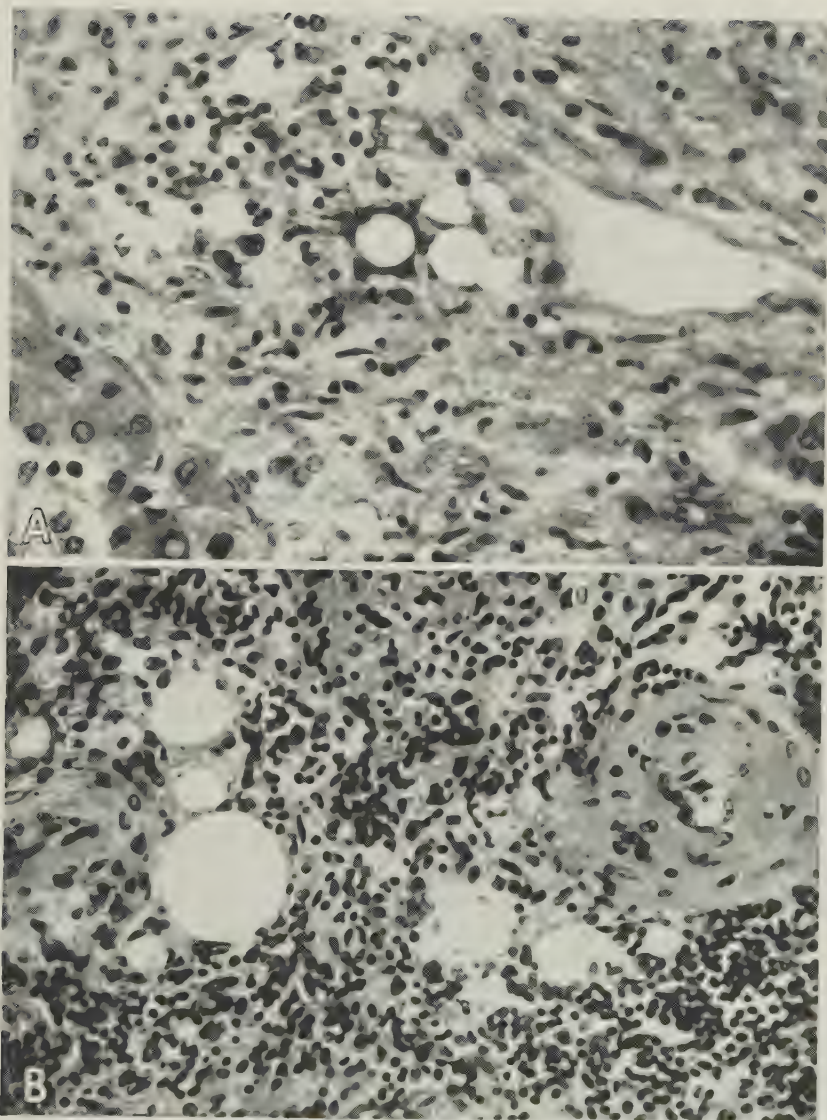


Fig. 4.—*A*, portal triad of a patient who had suffered from constipation for many years and had used numerous cathartics. Oil is present both in macrophages and in extracellular collections; lymphatic cells are adjacent. $\times 459$. *B*, spleen of a patient in whose clinical history the bowel movements were described as regular. The oleophages and larger collections are adjacent to the central arteries of the malpighian corpuscles. $\times 306$.

addition to the 23 cases there were 7 instances in which sections of the liver showed vacuolated cells in or near the triads; it is possible that the mesenteric lymph nodes in these cases would have shown the lesions.

The clinical histories of the 23 patients in whose mesenteric lymph nodes the oleophages were found were studied; the correlation between the clinical histories and the microscopic changes is:

Clinical History	Oleophages Present
Liquid petrolatum used.....	5
Laxatives used for constipation.....	7
Use of laxatives denied.....	4
Clinical history not known.....	7

The history obtained in one of the cases of this group is given:

CASE 1.—A man of 49 years was admitted to the hospital with the diagnosis of subacute bacterial endocarditis. He remained in the hospital until his death, a total of one hundred and eight days. In the "inquiry by systems" on admission, it was noted that the patient suffered from occasional constipation and that he took liquid petrolatum every morning. During the one hundred and eight days in the hospital he received a total of 1,530 cc. of liquid petrolatum and 1,335 cc. of liquid petrolatum emulsified with agar. The amount given the patient varied from day to day; up to 60 cc. of oil was given on some days, while on other days smaller amounts of oil or of oil emulsified with agar were given.

At autopsy the clinical diagnosis was confirmed. Microscopic examination of the colon revealed in the basal portion of the lamina propria a few scattered vacuolated cells, the vacuoles unequal in size. No giant cells were seen. In the mesenteric lymph nodes were numerous vacuoles inside and outside cells. Most of the vacuoles were located either in peripheral lymphatic follicles or in medullary cords, but a few appeared to be in the central sinuses. About some of the larger extracellular vacuoles were clusters of smaller vacuoles. Six of the mesenteric lymph nodes were examined, and these oleophages were found in all, but the quantity varied in each lymph node, some sections showing many intracellular and extracellular vacuoles and others showing only one or two small vacuolated cells. In the liver many of the triads contained small collections of vacuolated cells similar to those seen in the colon, and similar groups were found focally in some of the lobules. These cells were surrounded by small lymphatic cells. The triads all contained an increased number of round cells. In many of the malpighian corporcles of the spleen were collections of vacuolated cells similar in all respects to those in the liver. No extracellular vacuoles were seen.

Frozen sections of the colon stained with sudan IV revealed much more sudanophilic material in the lower portion of the mucosa than was indicated in the hematoxylin-eosin sections. This material failed to reduce osmic acid; when stained with the Carminati stain it was yellow, in sharp contrast to the orange color of the adipose tissue of the submucosa. The vacuolated areas in the mesenteric lymph nodes and in the hepatic triads contained material demonstrating the same reactions with osmic acid and orange sudan G as the material in the colon.

The appearance of the tissues in the other cases was essentially the same. However, in many of the lymph nodes numerous giant cells were

present, chiefly crescentic, surrounding the extracellular vacuoles, but occasionally appearing to lie free and resembling the Langhans type of cell.

In order to determine more definitely any frequency of absorption of liquid petrolatum in human subjects, the mesenteric lymph nodes, livers and spleens from 25 consecutive autopsies performed at Albert Merritt Billings Hospital on bodies over 21 years of age were examined. Since the previous work had indicated that lesions in the intestine would be present only in the event of marked changes in the mesenteric lymph nodes, microscopic examination of the intestines was made only in the cases in which oleophages were observed in the lymph nodes. These tissues were examined without knowledge of the use of laxatives during life; but subsequently the histories were studied.

The correlation between the patients' histories as regards the use or possible use of liquid petrolatum and the microscopic observations is:

Clinical History	Oleophages Present	Oleophages Not Found
Liquid petrolatum used.....	7	4
Laxatives used for constipation.....	4	2
Use of laxatives denied.....	1	4
Clinical history not known.....	3	

The history obtained in 1 of the cases of this group is as follows:

CASE 2.—A man of 54 years was admitted to the hospital with the diagnosis of carcinoma of the lung. In the "inquiry by systems" it was noted that the patient suffered from mild constipation. During the sixty-eight days that he was in the hospital he received a total of 1,440 cc. of liquid petrolatum.

Autopsy confirmed the clinical diagnosis. Microscopic examination of the intestines revealed no abnormalities. Scattered throughout two of the three mesenteric lymph nodes examined, lying in the peripheral lymphatic follicles and the medullary cords, were nests of vacuolated cells and large extracellular vacuoles similar to those previously described. In apposition to some of the larger vacuoles were crescentic giant cells with eosinophilic cytoplasm; in some of these giant cells vacuoles could be seen. In some of the follicles were nests of eosinophilic mononuclear cells showing no vacuolation. Frozen sections of the lymph nodes revealed the vacuolated areas to contain a sudanophilic material, which failed to reduce osmic acid and which stained yellow with the Carminati stain in contrast to the orange color of the surrounding adipose tissue. In the liver some of the triads contained cells with small vacuoles of varying size, surrounded by lymphocytes. Frozen sections revealed a sudanophilic material, part of which reduced osmic acid, while another part failed to reduce it. With the Carminati stain, no evaluation could be made of yellow-staining material in the triads because of lack of contrast with the surrounding liver cells and red blood cells. In several of the malpighian corpuscles of the spleen were small nests of vacuolated cells similar to those in the liver and lymph nodes. No extracellular vacuoles were seen. In frozen sections the sudanophilic material in these cells stained irregularly, some reducing osmic acid and other portions not reducing it, and some parts staining yellow and other parts orange with the Carminati stain.

In this study of human tissues there was found only partial correlation between the clinical histories and the microscopic changes; in about one third of the 25 consecutive cases the microscopic observations were directly opposite to what the clinical histories suggested. There are at least two possible factors in this lack of correlation. Many of the clinical histories are doubtless inadequate; many patients do not regard liquid petrolatum as a laxative, and unless specific inquiry is made its use will not be mentioned. A second factor is technical; it was found in this study that if several of the mesenteric and hepatic hilar lymph nodes from the same person were examined, macrophages containing oil might be present in some of the nodes while the remaining nodes appeared normal. Thus in some of the cases in which oil was not observed examination of other nodes might have permitted a different conclusion.

In 15 of the 25 consecutive autopsies, or 60 per cent, the lymph nodes revealed the presence of oil. This percentage might have been even greater if more nodes had been examined in some of the cases in which presence of oil was reported not found. In 6 cases, or 24 per cent, there were sufficient oleophages to warrant a ++ or greater grading. In 4 livers, or 16 per cent, oil was demonstrable by microscopic examination. No oleophages were found in any of the sections of intestines. In 6 cases, or 24 per cent, there were vacuolated macrophages in the spleen. Pinkerton and Moragues²⁷ recently described the presence of similar cells in the spleen and liver in a case of paraffinoma of the lung; in the cases of pneumonia due to aspiration of liquid petrolatum observed in this laboratory the findings have been similar. Thus there are two possible sources for the splenic and hepatic lesions. In the cases in this series, however, the cells were present in the mesenteric lymph nodes whenever they were present in the liver and spleen, and no similar cells were seen in the lungs.

These findings in the human subject are similar to those in the experimental animal. The human subject first shows lesions in the mesenteric lymph nodes; lesions in the intestines are not frequent but may be present in cases of ingestion of liquid petrolatum over a long period. Giant cells are much more frequent and conspicuous in the human subject, but in other respects the location and morphologic character of the lesions are the same.

CHEMICAL ANALYSES

In an attempt to recover any liquid petrolatum that might be present in the various organs, some of the tissues were chemically analyzed. There were two main reasons why such a procedure seemed desirable. Although the appearance of the oleophages could be considered

27. Pinkerton, H., and Moragues, V.: *Arch. Path.* **29**:691, 1940.

characteristic of oil absorption, and the various staining methods gave supporting evidence concerning the nature of the contained material, it was felt that more conclusive proof would be available if a substance similar to liquid petrolatum could be recovered from the tissues. Chemical analyses would also provide information as to the extent to which absorption of this oil could occur quantitatively. This portion of the work was done under the direction of and with the assistance of D. Warren Stanger, of the Otho S. A. Sprague Memorial Institute.

The method used consisted of two parts: (1) the determination of the percentage of the unsaponifiable fraction of the test and of the control tissue and (2) the separation of the various components of the unsaponifiable fraction by chromatographic adsorption.²⁸ To determine the unsaponifiable residue the macerated tissue was saponified in alcoholic potash (a solution of potassium hydroxide in 95 per cent alcohol), extracted with ethylene dichloride and the solvent evaporated by vacuum distillation until the residue attained a constant weight. This residue was again saponified and extracted. The fractionation of the various components of an unsaponifiable mixture of materials soluble in fat solvents by chromatographic adsorption is based on the differing affinity possessed by activated aluminum oxide for the various components. In general, the more saturated the substance the less tendency will it have to be adsorbed to the particles of aluminum oxide, and compounds with certain active groups, such as the sterols, will have more tendency to be adsorbed than will the unsaturated hydrocarbons. In a mixture of cholesterol, carotene and liquid petrolatum there will be no adsorption of the saturated hydrocarbon and the carotene will be displaced by the cholesterol. Thus, if a mixture of the three fractions dissolved in purified petroleum benzine U. S. P. (petroleum ether) is poured into a column of activated aluminum oxide, the liquid petrolatum will be found in the lower portion of the column, the carotene in the center and the cholesterol nearest the top. Since the carotene is a colored substance, it will provide a line of demarcation between the other two fractions. When the column has been washed sufficiently to drive the carotene line toward the bottom, it will be known that all the liquid petrolatum is in the solvent in the flask below the column and that the cholesterol is attached to the aluminum oxide above.

The usefulness of this method was tested by a preliminary experiment in which weighed amounts of liquid petrolatum and cholesterol were dissolved in purified petroleum benzine, a minute amount of carotene added and the solution fractionated by use of the column of activated aluminum oxide. The results were as follows:

	Amount Used	Amount Recovered
Cholesterol	1.0027 Gm.	
Liquid petrolatum.....	0.0994 Gm.	0.0992 Gm.

Thus 99.8 per cent of the liquid petrolatum used was recovered.

Rabbit, rat, guinea pig and human tissues were analyzed by this method. The complete details of a typical analysis are:

Rabbit 29: A description of the feeding and the gross and microscopic observations on the tissues of this animal have been given. For the chemical analysis

28. Zechmeister, L., and von Chohnoky, L.: Die chromatographische Adsorptionsmethode, Berlin, Julius Springer, 1938.

of the liver, 92.8 Gm. of wet tissue was available. To this, after its maceration in a food chopper, was added 115 cc. of 6 per cent alcoholic potash, and the mixture was heated on the steam bath for eight hours. Then 60 cc. of distilled water was added, and the unsaponifiable material was extracted with 150 cc. of ethylene dichloride. The extraction was repeated three times, with 75, 75 and 50 cc. The water was then removed with anhydrous sodium sulfate, and the ethylene dichloride was evaporated by vacuum distillation until the residue had been brought to a constant weight. The weight of the unsaponifiable residue was 3.919 Gm. To this was added 15 cc. of 6 per cent alcoholic potash, the mixture heated as before and 20 cc. of distilled water added. Extraction was done with 25, 15, 15 and 15 cc. of ethylene dichloride. The water was again removed with sodium sulfate, and the ethylene dichloride was distilled from the residue. The weight of the unsaponifiable residue was then 2.9077 Gm. This material, which had an oily appearance, was dissolved in an excess of purified petroleum benzene, and to the solution a small amount of carotene was added. Not all of the residue was soluble, and only the supernatant fluid after centrifuging was poured through the column of activated aluminum oxide. After all of the solution had been added, the column was thoroughly washed by an excess of purified petroleum benzene. The solvent was evaporated by vacuum distillation until the residue attained a constant weight. The material thus recovered was clear and colorless and had the same appearance as the liquid petrolatum originally used. The amount recovered was 2.4517 Gm., which was 2.64 per cent of the wet weight of the liver.

The physical and chemical properties of this unadsorbed residue isolated from animals fed only one type of liquid petrolatum were determined and were compared with the corresponding properties of a fresh sample of the oil. The results were as follows:

	Index of Refraction at 23 C.	Specific Gravity at 30 C.
Unadsorbed residue.....	1.4690	0.8528
Light liquid petrolatum.....	1.4718	0.8587

The physical properties showed marked similarity. In the matter of specific gravity, the difference between that of the material isolated from the tissues and that of the fresh sample is only 0.0059; the range given by the manufacturers for the type of oil used is 0.0100. Thus the difference found here is about one half of that possible, according to the specifications of the oil. The oil used in feeding the animals was purchased at varying periods and was not all from the same lot, as was the fresh sample tested.

The chemical property determined was the absorption of hydrogen:

	Hydrogen Absorbed per Gram of Material, Standard Conditions
Unadsorbed residue.....	3.379 cc.
Light liquid petrolatum.....	1.052 cc.

A greater amount of hydrogen was absorbed by the final residue, but this included the hydrogen taken up by the material other than liquid petrolatum; the amount of hydrogen actually absorbed was very small, and this indicates that the product isolated from the tissues was practically saturated.

The technic of the analyses of the other tissues was similar to that described in all details. The results of the various analyses are given (all figures are the percentages of the wet weights of the tissues):

Rabbits.—Rabbit 29: This animal was fed liquid petrolatum for thirteen months. The details of the feeding and the results of the microscopic examination have been given. To make more certain that none of the material recovered was material adherent to the surface of the mucosa, the animal was fed the regular diet without the liquid petrolatum for three weeks before being killed.

Rabbit 33: This normal adult rabbit was used for control tissues.

	Unaponifiable Residue (%)	Unadsorbed Residue (%)
Rabbit 29, intestine.....	2.85	2.24
Rabbit 33, intestine.....	0.45	0.02
Rabbit 29, liver.....	3.13	2.64
Rabbit 33, liver.....	0.45	0.04

Rats.—Rats 17 and 20: The tissues from these two animals were used together. Both animals had been fed on the bread and liquid petrolatum diet as previously described—rat 20 for six months and rat 17 for nineteen months. The feeding and the microscopic observations have been described.

Rats OC and YC: These are the control animals of the second group of rats, receiving no liquid petrolatum.

	Unaponifiable Residue (%)	Unadsorbed Residue (%)
Rats 17 and 20, liver.....	8.60	6.37
Rats OC and YC, liver....	0.57	0.03

Rats OT and YT: The tissues from these animals were used together. These rats were members of the second group, which had been fed 5 per cent liquid petrolatum mixed with their diet for six weeks.

Rats OC and YC: The tissues from these animals were also used together. These were the control animals of the second group and received no liquid petrolatum.

	Unaponifiable Residue (%)	Unadsorbed Residue (%)
Rats OT and YT, liver...	0.92	0.48
Rats OC and YC, liver...	0.57	0.03

Guinea Pigs.—Guinea pigs 2, 5, 18, 30, 36: Since only small portions of tissue fixed in solution of formaldehyde were available from the test animals, the tissues from the 5 guinea pigs were combined. These animals had been fed for periods varying from eight to fifteen months. The amount of oil given ranged from 800 to 1,200 cc.

Guinea pig C: The control animal was selected from a group which had been fed the stock laboratory diet.

	Unaponifiable Residue (%)	Unadsorbed Residue (%)
Guinea pigs 2, 5, 18, 30, 36, liver...	0.43	0.054
Guinea pig C, liver.....	0.29	0.007

A close correlation exists between the microscopic observations and the results of the chemical analyses. In those tissues in which many

macrophages containing oil were demonstrable, the quantity of the final unadsorbed residue, probably chiefly oil, was from one hundred to two hundred times as great as the unadsorbed residue of the control tissues. The results of the experiment with the rats fed liquid petrolatum for only six weeks deserve special note. After this comparatively brief period on a diet containing 5 per cent of liquid petrolatum, the livers contained sixteen times as much residue as did the livers of the control rats. In the livers of the test rats no microscopic lesions were demonstrable; the oil was probably in too small quantities in individual macrophages to be recognized. That this may be true of many other tissues can only be suggested.

In the control tissues a very small quantity of residue not adsorbed to the aluminum oxide is present. The determination of the exact chemical nature of this material is beyond the scope of this investigation; its presence does not alter the conclusions.

Man.—In the interpretation of the results of the analysis of human tissues for ingested liquid petrolatum, no value can be given to the clinical histories regarding any use of the oil. The microscopic examination of human tissues showed that typical macrophages containing oil were present in the mesenteric lymph nodes and other tissues of patients who had not mentioned any use of laxatives. Thus it is difficult to obtain satisfactory control tissues. The use of the tissues of an infant dying before any liquid petrolatum is likely to have been given is not possible, because in the analyses of the tissues of the control rats it was found that there is an increase with age in the quantity of the unsaponifiable and unadsorbed residues. Despite this difficulty, analyses were made of the livers of two adults.

1. The details of this case have been given on page 686. There is a positive history of the use of liquid petrolatum, and the typical oleophages could be demonstrated microscopically in the liver.

2. The other patient was a girl of 22 years who died of chronic glomerulonephritis. The use of any laxative was denied; none was administered during the brief hospitalization, and no evidence of absorption could be seen on microscopic examination of the liver.

	Unsaponifiable Residue (%)	Unadsorbed Residue (%)
1. Liver	0.632	0.102
2. Liver	0.534	0.011

The demonstration of ten times as much unadsorbed residue in the test tissue as in the control seems to be significant. However, study of a larger series of cases would be necessary before definite conclusions could be drawn.

COMMENT

The results of these investigations demonstrate that liquid petrolatum is absorbed in small amounts from the intestines in human subjects and in experimental animals. This can be shown both by microscopic examination of the mesenteric lymph nodes and, in certain cases, of the

intestines, liver or spleen, and also by chemical analysis of the tissues. As a foreign body, the oil present in the tissues initiates a characteristic reaction. By morphology and staining methods, this lesion can be differentiated from the pathologic changes associated with the deposition of endogenous fats and lipoids. In the present work, as in that of Twort and Twort,¹³ the ingested material was found in phagocytes. Tantini's¹⁴ observations that the oil was stored in parenchymatous cells were based on the use of the Carminati stain. The lack of specificity of this stain as applied to hepatic tissue invalidates his conclusions. Both Twort and Twort and Tantini observed lesions only in the liver.

The results of the chemical analyses of the various tissues corroborate the conclusions of Channon and Collinson.¹² It is of additional interest that two different methods of analysis gave essentially the same results.

The method of absorption of the oil has not been demonstrated. Since liquid petrolatum is unsaponifiable, its absorption must be by a process other than that characteristic of ordinary fats and oils.

Pathophysiologic effects of the deposition of liquid petrolatum were not noted. The eventual reaction of the tissues to the presence of liquid petrolatum might vary. In pneumonia due to aspiration of liquid petrolatum and about paraffinomas in many locations there frequently occurs marked fibrosis of the surrounding tissues. Whether a comparable reaction occurs in the intestinal mucosa, the mesenteric lymph nodes, the liver or the spleen cannot be stated. The pathologic changes known to result from the presence of liquid petrolatum in the lumen of the intestine²⁹ were not observed in these experiments, probably because special precautions were taken to supply a diet rich in vitamins.

SUMMARY

Liquid petrolatum is absorbed in small amounts from the intestines of human subjects and experimental animals. The oil is demonstrable most readily in the mesenteric lymph nodes but may be present also in the intestinal mucosa, liver and spleen. A substance similar to liquid petrolatum in physical and chemical properties can be recovered from the unsaponifiable fraction of the involved tissues of animals fed this oil.

Liquid petrolatum is a foreign body in the tissues and excites a typical reaction, characterized by cells of chronic inflammation, including giant cells.

Pathophysiologic effects attributable to the deposition of liquid petrolatum in the tissues have not been demonstrated in this investigation.

I wish to express my appreciation to Dr. H. Gideon Wells for kind assistance and helpful suggestions during the progress of this investigation.

29. Jackson, R. W.: *J. Nutrition* **4**:171, 1931. Curtis, A. C., and Kline, E. M.: *Arch. Int. Med.* **63**:54, 1939. Elliott, M. C.; Isaacs, B., and Ivy, A. C.: *Proc. Soc. Exper. Biol. & Med.* **43**:240, 1940.

